Critical Digest.

ANATOMICAL, PHYSIOLOGICAL AND PATHOLOGICAL NOTES.

ACROMEGALY.

By JOSEPH COLLINS, M.D.,

New York.

[*Concluded from January number.*]

Observation LXXVI.—(Long.) Male, German, aged forty-eight, good family history; denies syphilis; had always been well, except at the age of twenty-five, when, in the German army, he had an abscess on left hip which lasted for five weeks. Came to this country in 1870; married shortly afterward, and from this union were three children, two of whom died in infancy; the third is now a young man and perfectly healthy. Twelve years ago he had an abscess on right hip which was very severe, but he made a good recovery. The symptoms of acromegaly first made their appearance in the hands in 1874; he was then thirty-one years old. Since that time the growth has been constant Although he is but 5 feet 9½ inches in height, he weighs 262 pounds. The skin is of dirty yellow color. Hands, feet, and face enlarged; cranium normal in size; forehead retreating; hair thick and wiry; nose and lower lip very much enlarged; eyelids and upper lid normal. Marked prognathism; lower jaw greatly hypertrophied; tongue much enlarged; slight cervico-dorsal kyphosis; thyroid gland apparently normal. Hands and arms are typical, the right hand and foot slightly larger than the left. No post-sternal dullness. Genital organs apparently normal; sexual appetite diminished. The thorax, clavicles, and ribs partake of the hypertrophy. Knees and legs enlarged; feet enlarged, flat-footed.

Special senses normal with the exception of sight, which has been lost for ten years, and so completely that he has no perception of light. Eyeballs not greatly pronounced, but marked nystagmus and complete optic atrophy. Patient is of average intelligence, and there is no polyuria, polydipsia or bulimia; measurements given.

OBSERVATION LXXVII.—(Cenas.) A boy, aged fifteen. Mother, who was an alcoholic, died at forty-nine years of age; the patient the youngest of six children and the last child. The mother was drunk at least once a week while carrying this child, and had a tedious labor, lasting five days. Asymmetry of face was noticed at birth. Enlargement of hands and feet, and to some extent the arms, was remarked when the child was a few months old. The hands and feet continued to enlarge, as the child grew older, out of proportion to the other parts of his body. For past two years he has had frequent fainting-spells of a few minutes' duration. Intelligence less than is common to his age, and frequent headache. The face is round and asymmetrical; hands covered with large violet spots; head large and asymmetrical; feet enormous; forearms small; wrists small; fingers sausage-shape; nails thick and crooked; hands and arms not quite symmetrical; of the right hand all the fingers are affected; of the left, only the thumb and index finger. The legs, thighs, and knees are normal; all the toes of left foot are enlarged, but only the first, second, and fifth of the right are affected Similar spots on feet as on hands. Head large; marked prognathism of lower jaw; the teeth partake of the enlargement; right side of face larger; and like condition exists in right side of palate, cheeks, lips, and tongue. Thyroid body enlarged on right side. Slight cervico-dorsal kyphosis; no retro-sternal dullness. In lumbar region the skin shows signs of scleroderma. Penis markedly enlarged. Headache, vertigo, and fainting are troublesome. Special senses normal. Voice thick, harsh, and muffled; appetite and thirst increased.

This case has been given somewhat in detail, as it is reported as the only congenital case on record.

OBSERVATION LXXVIII.—(Gerhardt.) Male, aged sixty-two; no family history pertaining to the disease; he has been exposed greatly to inclemency of the weather, and a hard drinker. Has had gonorrhœa and syphilis, intermittent fever, and has suffered severely from bronchial catarrh. Symptoms began in 1888, with pain and swelling in left ankle; then it went to the other ankle, and later to the hands, the right hand being the most severely affected. The pains are intermittent; there is excessive sweating and thirst; the nails are striated and crack easily, and the terminal phalanges are greatly enlarged of the feet and hands.

[It is scarcely posssible from the description of this case to see just why it should be classified under acromegaly.]

OBSERVATION LXXIX.—(O'Connor.) Female, born in Ireland, aged fifty, no family history, and with the exception of attacks of headache was healthy during childhood; married at eighteen years of age, and afterward had an attack of yellow fever. First noticed that she was getting stout in 1883. The hands and feet felt as if bursting, the right hand being first affected, then the left foot. This sensation of fullness was also complained of in the throat. Then the nose began to get red and enlarged, and the voice harsh. The face became enlarged, both transversely and longitudinally lower lip thickened and curled, tongue immense. Hands and feet characteristic. The left foot shows a greater increase than the right, and it has a marked thickened pad beneath metatarsophalangeal region. No enlargement of the bones of the arms or legs. There are distinct circumscribed tumors on some of the bones, such as the seventh rib and the clavicle. The thyroid gland can be made out; she sweats profusely and has great thirst. The menopause occurred at forty-seven years of age.

OBSERVATION LXXX.—(Sommers.) Male, Italian, fifty-one years old; has had large hands and feet since he was twenty years old. They have greatly increased in size in recent years. In 1886 he had a chancre, but no secondary symptoms appeared. In 1870 he had an attack of small-pox. The voice is croaking; he is surly in disposition and very reticent. Forehead narrow, low, and retreating; frontal sinuses large; nose very large; ears immense; lips thick; tongue hypertrophied and deeply fissured; marked prognathism of lower jaw; hands typical in shape, the width and thickness of fingers out of all proportion to the length; palms covered with great pads of tissue, more marked on ulnar side. The enlargement of the feet is of the same character as seen in hands. The great toe is enormous; patellæ are immense; knee-joints crepitate; very slight kyphosis. He weighs 275 pounds, though but 5 feet 11 inches in height. Thyroid small, special senses normal. At the autopsy, the brain and spinal cord was not examined. There was found fatty and cirrhotic liver, enlarged spleen, and absence of thymus.

OBSERVATION LXXXI.—(Bruzzi.) Male, age fifty-one, unmarried, of good family and previous history.

No illness of importance in childhood; had spermatorrhœa when a young man. He was of good constitution and development, and performed military service. When twenty-six years of age he had attacks of severe pain in back of head and neck and the dorsal region. At twenty-nine years of age he was impotent, and the pains were troublesome, and he had an attack of nervous prostration. In 1870 he had an attack of prostration, with delirium and a tendency to coma, in which he remained in an unconscious condition for forty days. His physician diagnosed this as cerebral congestion. After a long convalescence he regained strength, but was troubled with aggravated attacks of dyspepsia. The signs of acromegaly were quite typical, but not of a marked order. Prognathism and kyphosis were not well marked. A full table of measurements appended to original paper.

OBSERVATION LXXXII.—(Gajkiewiczi.)

OBSERVATION LXXXIII.—(Gause.)

These reports are inaccessible in the time necessary to complete this article. Dercum reported two cases to the American Neurological Association in June, 1892, which have not as yet been published.

Foy has reported a peculiar case, which I have included under this heading for the purpose of drawing attention to local manifestations resembling acromegaly, and to which he has given the name cheiromegaly. The case is in brief as follows: The patient, a refined lady, had had small ecchondromata removed from her hand twelve months before, and presented herself for the removal of a second such tumor, about the size of a large hen's egg. Shortly after the removal of the second tumor, a strange alteration occurred in the hand; it became broad and large, and very much resembled the hand of acromegaly, but unattended with any other changes or concomitants of acromegaly. The patient died afterward, but from what cause the reporter does not mention.

As yet the most obscure factors concerning acromegaly are the causation and pathology of the disease. As we have already stated in the beginning of this article, its occurrence has been attributed to various factors without its being in any particular instance shown to be dependent upon the attributable causes. Although the majority of the cases have been observed in persons occupying the most lowly walks of life, we cannot say that it is a respecter of persons, for it has been observed in clergymen, officers, and the refined and educated.

Regarding the theories of its pathology, the one looked to with most unanimity is that promulgated by Marie, who is particular to confess that the nature of the disease is wrapped in obscurity, but that the cases which have come to autopsies have shown, with considerable concordance, changes in the pituitary body. Many of the cases still under observation present symptoms, as can be seen in our abstracts of them, which point with a considerable degree of accuracy to an involvement of this body. In more than one-half the cases reported, eye or ear symptoms, pointing to the pituitary body, have been present and headache in almost every case. What this change in the hypophysis cerebri is, only time and detailed examinations will show. At the same time it is interesting to note instances where the pituitary body has presented changes in conjunction with other diseases without any symptoms of acromegaly developing. Such a case has recently been reported by Wills ("Brain," autumn and winter number, 1892). This patient had pains in the head for fifteen years, which were greatly increased in severity during the last six months. With the exception of progressive dementia, the symptoms were not well marked. There was some paresis of the left internal rectus muscle of the right eye with external strabismus; the other muscles of this eye were normal. Right pupil reacted to light and accommodation, the left to neither; consecutive optic atrophy in both discs. After death a tumor, about the size of a Tangerene orange, divided into two portions, was found wedged in the sella turcica. It lay in the interpeduncular space, extending anteriorly as far as the posterior termination of the orbital surface of the frontal lobes, and laterally it was overhung by the tempero-sphenoidal lobes. Posteriorly it separated the crura cerebri. Anteriorly the olfactory nerves were thin and flattened, the left more than the right, and likewise the optic tracts were more involved on the left side. Microscopical examination showed it to be an adenomata.

Boyce and Beadles have likewise reported three cases in which there was enlargement of the thyroid without symptoms of acromegaly (Journal of Pathology, 1892). Two of these cases were of myxœdema. and one of sporadic cretinism, and associated with the enlargement of the hypophysis was an atrophied condition of the thyroid glands. Suckling has also seen the same condition in a case of myxœdema.

It has been suggested that in acromegaly the changes in the pituitary and thyroid glands stand in relationship one to the other; that is, when the latter is absent or diminished in size the former is hypertrophied. It has been shown experimentally by Hofmeister (Fortschritte der Medicin, No. 4, 1892) and others that after thyroidectomy in rabbits the hypophysis increases in weight; but these experiments have not been corroborated in every instance by other workers in the same line. In acromegaly many of the cases, such as Hudden's, Ballance's, Virchow's, Kanthack's, and others, there was atrophy of the thyroid gland, while in others the gland remained normal or was hypertrophied.

The functions of these two bodies, the thyroid and hypophysis, have yet to be learned; there is no doubt, as has been shown by Rogowitsch, that an intimate connection exists between them and that they stand in a close relationship with the nervous system, particularly the sympathetic. That one should take up the function of the other when diseased is comprehensible even when experiments fail to show that change goes on in the pituitary body after extirpation of the thyroid. The fact that acromegaly does not develop in every case of tumor of the hypophysis cerebri cannot be logically advanced as an argument that its normal existence does not prevent acromegaly; for we know that disease of the spleen is attended with the development of leucocythæmia, yet leucocythæmia does not necessarily follow extirpation of that organ. Nor does myxœdema necessarily accompany disease of the thyroid gland, although in bodies of persons dead from myxœdema, the thyroid is invariably degenerated and generally atrophied.

If acromegaly is dependent on disease of the pituitary body, it does not necessarily follow, as I have before stated (American Neurological Association meeting, June, 1892), that there must be enlargement or tumor of that body. There may be atrophy or parenchymatous degeneration; for if we accept that disease of the pituitary gland has a causative relation to acromegaly, it must be in either one of two ways: Either the pituitary gland —the prehypophysis, so called—secretes and pours out into the circulation certain substances necessary for the preservance of proper nutrition, and the absence of which is manifested by changes in the general system through the nervous system, particularly the sympathetic; or the normal pituitary gland filters out of the blood certain substances the retention of which would give rise to a sort of toxæmia, the consequences of which would be a deleterious action on the nervous system and the resulting changes of the disease. Why there should be a special predilection for the extremities would have to be explained by some conditions of peculiarity of the circulation influenced through the vaso-motors.

It will be seen, from a glance at the literature for the past two years, that the disease known as acromegaly has come to stay, and that a diffusion of knowledge concerning its occurrence is followed by the report of many cases formerly classified under some other heading, but clearly belonging to acromegaly.

Acromegaly is most easily confounded with the disease known as osteo-arthropathy hypertrophica pneumique: a disease characterized by enlargement and deformity of the extremities, particularly at the joints, and dependent on some pulmonary disease, most often of a septic nature. It may also be confounded with myxœdema, leontiasis, oteitis deformans of Paget, elephantiasis, erythromelalgia, and rarely, if ever, with arthritis deformans.

In acromegaly the hands are large and thick in appearance, the fingers are uniformly enlarged, and the proportion between the segments of the fingers is well preserved. The nails are flat, small, longitudinally striated, and the flesh has a tendency to grow beyond and around, seemingly imbedding them. In osteo-arthropathy of pulmonary origin, the fingers, and not the hand as a whole, are affected. The fingers assume the shape of drum-sticks, and the ends of the bones of the forearm are markedly thickened, projecting voluminously on the dorsal surface of the hand, and the hand, as a whole, shows very evident deformity. The nails become changed, so that they resemble a parrot's beak. This last is a very important factor, and will suggest the diagnosis very quickly; for while, in acromegaly, there is great enlargement, there is no actual deformity, as the relationship between the different parts of the hand is well preserved, and the hypertrophy of the wrist is proportionate to that of the hand in acromegaly. In acromegaly the carpo-metacarpal region is very greatly enlarged, giving rise to the so-called "battledore" hand, while in osteo-arthropathy this articulation is nearly normal. The same remarks apply to the feet, excepting that there the changes are a little less marked. Another very important difference is that, in acromegaly, the changes are equally in the bones and soft tissues, while in osteo-arthropathy the alterations are only in the bones. There are certain parts of the bone—namely, the epiphysis—where a marked predilection exists for these changes.

In acromegaly the face undergoes an important change. There is enormous hypertrophy of the inferior maxilla, and this gives a characteristic prognathous appearance. In osteo-arthropathy the lower jaw is never affected, with the exception of occasional thickening of the alveolar border in both inferior and superior maxillæ. Acromegaly is attended with a more or less well-marked cervico-dorsal kyphosis, which develops early; while such a change, if it occurs at all in osteo-arthropathy, is a late manifestation.

In acromegaly there are frequently symptoms referable to the eyes and ears, indicative of change in the pituitary body or adjacent to it; while such symptoms do not exist in osteo-arthropathy. Two very constant accompaniments of acromegaly are the development of little nodules of molluscum fibrosum and a large welt of thickened tissue on the inner side of the plantar surface of each foot. These have not been noted in osteo-arthropathy.

Finally, osteo-arthropathy is always secondary to pulmonary disease, and particularly, as has before been said, pulmonary diseases attended with the production of pus, such as phthisis tuberculosis, empyæmia, pulmonary abscess, and the like.

The decomposition of pus would seem to be the necessary antecedent for the development of the osteo-arthropathy, the morbid changes being brought about by the absorption of the products of such decomposition. The *locus* of such purulent change being in the lungs, would seem to facilitate, in some unknown way, the development of the osteo-arthropathy. In this disease, likewise, there has been found quite a hereditary element; while in acromegaly, on the other hand, the origin of the disease is in entire obscurity, and, with one possible exception, the disease has shown no hereditary factors in its etiology.

The differential diagnosis from myxœdema is generally not difficult. In myxœdema the face is of a characteristic " full-moon " appearance; the skin is of a peculiar waxy color, with a pinkish tint in cheeks; mentality is sluggish; the chin drops forward on the sternum from sheer inability on the part of the extensors of the head; the skeleton remains free from enlargement. In acromegaly, on the other hand, the outline of the face is elongated; there is marked prognathism; the skin is thickened and muddy-looking; the patient is frequently very alert mentally (Cohen's case); and remarkable changes go on in the skeleton. In myxœdema there is absence of secretion of sweat and early alopecia; while in acromegaly there is hyperidrosis and thick, tough, wiry hair.

In Paget's disease (osteitis deformans) the bony changes in the upper part of the skeleton are most marked in the cranium. The outer table of the cranial bones becomes porous and spongy, as a result of inflammation, and the normal distinction between the outer table and the inner table and diploë is lost, the entire thickness of the bone consisting of a uniformly compact tissue, in some parts looking like chalk. The bones of the face are but slightly affected, and then only late in the disease; while in the long bones the changes in size and curvature are principally in the shafts, the extremities being scarcely affected. It will be readily seen that these are in marked contrast to the conditions present in acromegaly.

Arthritis deformans, leontiasis, and elephantiasis will scarcely be confounded with acromegaly, if the latter is carefully studied. In leontiasis ossium there is a growth of true bony structures in the shape of tumors of the cranium and face, and generally an absence of hypertrophy of the extremities. In arthritis deformans the changes are confined to the joints of the extremities, the face being rarely affected, and never does it present the elongated face of acromegaly. Elephantiasis consists of cystic and tubular enlargements of the lymphatics—first, of the cutaneous structures, then of the more deeply seated, attended with thickening and induration of the skin and connective-tissue and dilatation and multiplication of the blood-vessels, with wasting of the muscles, and attended with no change in the bony structure. A disease presenting these conditions will scarcely be confounded with acromegaly. Souza-Leite informs us that it is possible to confound acromegaly with the disease to which Weir Mitchell gave the name of erythromelalgia —a word signifying literally pain and redness in a limb. The disease in question is, however, only occasionally attended with an increase in the size of the fingers and hands and a slight fullness of the arms and forearms, and rarely a small degree of kyphosis.

There is, moreover, to assist us in the differential diagnosis, an absence of elongated face and prognathism of the lower jaw, of the enlargement of the lips and tongue, and, in fact, of all the signs referable to the cephalic extremity so apparent and characteristic of acromegaly. Although enlargement of the extremities may occur in erythromelalgia, it is due to congestion and œdema, and the changes in the fingers, nails, and extremities, so typical in acromegaly, are absent.

Though much new material has been given for observation during the past two or three years, scarcely anything has been added to our knowledge of the causation and nature of the disease and its treatment. Undoubtedly the prognosis in this disease is extremely bad as regards complete recovery, but so few cases have as yet been described from the pathologist's point of view, the disease has not yet been recognized sufficiently long for us to give definite ideas as to its natural duration. It is probably, however, not less than a decade and longer in the greater number of cases. In one case (Bury) the duration of the disease was but three years, while in another (Graham) thirty-four years passed before death occurred. On account of our ignorance of the genesis of the disease, the treatment must be empiric and symptomatic. There has but little been suggested in a therapeutical way since the appearance of Souza-Leite's brochure, in which it is stated that Verstraeten has prescribed in this affection: phosphorus, perchloride of iron, arsenic, rhubarb, etc., and has placed patients on a modified Oertel's regimen, and other plans, but with little promise of success. In a few cases there is an amelioration of some of the symptoms, while other symptoms remain the same or are exaggerated.

Brown has recently stated that his patient was improving under the use of antipyrine and arsenic. Massalonga states that the activity of the disease was held in check by the administration of the salicylates and iodides. For the intense cephalalgia preceding marked manifestations of the disease, and likewise present in the earlier part of the disease, valerianate of caffeine and phenacetine have been found of great service. In cases presenting symptoms of intra-cranial pressure, particularly ocular symptoms, iodide of potash has been given very largely, but without apparent benefit.

The symptomatic treatment consists in combating the headache, overcoming the glycosuria when it exists, and attention to the bulimia, polydipsia, and hyperidrosis, which are frequently troublesome. The glycosuria is generally combated readily by paying attention to the diet and the administration of arsenic and the alkaline waters.

All writers have been impressed with the necessity of paying attention to the nutrition of the patient from the beginning. The cause of death, in all cases reported as terminating fatally, has been asthenia, from intracranial pressure or from intercurrent acute diseases. The establishment of a high grade of nutrition will prevent these from occurring to some extent, especially the first and the last. Further than this, treatment seems to be of no avail.

Before closing, it might be well to remark that among English writers there might be a little more unanimity in the spelling of the word which Marie gave to the disease known by his name. There can scarcely be any excuse for writing it, as has been done by a recent writer (Wills), "acromegale;" and the substitution of a *k* for a *c*, in the first syllable, is merely a subserviency to the German, which is unnecessary. The appended bibliography brings the literature of the disease up to the date.

LITERATURE OF ACROMEGALY.

1772. Saucerotte: Observation communicated to Acad. de Chirurgie in 1772.
1801. Mélange de Chirurgie, 1801. Part i., p. 407.
1822. Alibert: Précis théorique et pratique des Maladies de la Peau. Paris, 1822. T. iii., p. 317.
1857. Chalk: Trans. Path. Soc. of London, 1857. Vol. viii., p. 305.
1864. Verga: Caso singolare de Prosopectasia in Rendiconti del Reale Instituto di Scienze e Lettere. Adunanza del 28 Aprile, 1864.
1868. Friedreich's: Virchow's Archiv. Vol. xlvii., p. 83.
1869. Lombroso: Le Giornale Ital. delle Mallattie Veneree, etc. Also, Virchow's Archiv. Vol. xlvi., 1869, p. 253. 1868.
1872. Ewald: Virchow's Archiv. Vol. lvi., 1872.
1877. Brigidi: Societa medico-fisica Fiorentina. Aug. 26, 1877.
1879. Faruffi: Annali Universali di Medicina, 1879. Vols. ccxlvii. and ccxlix.
1882. Henrot: Notes de Clinique médicale, Rheims, 1877; et Notes de Clinique médicale, Rheims, 1882.
1884. Fritsche and Klebs: Klinische und pathologisch-anatomische Untersuchungen. Leipzig, 1884.
1885. Hadden and Ballance: Transac. Clinical Society. London, 1885, vol. xviii.; also, *loc. cit.*, vol. xxi.
1885. Wadsworth: Boston Med. and Surg. Journal. Jan. 1, 1885.
1886. Marie: Rev. de Méd. Paris, 1886. vi., 297.
1887. Minkowski: Berlin. klin. Wochenschr. 1887, No. 21.
1888. Bier: Mittheilungen aus der chirurg. Klinik zu Kiel. Bd. iv., 1888.
1888. Golee: Brit. Med. Journal. 1888.
1888. O'Connor, J. T.: N. Am. Journal Homœop. New York, 1888, 3, s. iii., 345.
1888. Fraentzel: Deutsche med. Wochenschr. Aug. 9, 1888.
1888. Adler: Boston Med. and Surg. Journal. 1888, vol. cxix., p. 507.
1888. Wilks: Clinical Society of London. April 13, 1888.

1888. Marie: Nouvelle Iconograph. de la Salpêtrière. Paris, 1888, Nos. 5 and 6, part i.

1888. Lancereaux: Traitéd' Anatomie pathologique. Vol. iii.,part i.,p.29.

1888. Broca: Archiv. gén. de Méd. Paris, 1888, p. 656.

1888. Elliott: Lancet. 1888.

1888. Erb: Deutsches Archiv f. klin. Med. 1888, lxii., f. iv., 296.

1888. Tresilian: Brit. Med. Journal. 1888, p. 642.

1889. Virchow: Berlin. klin. Wochenschr. Feb. 4, 1889. Translated in Illustrated Medical News, London, 1889, vol. ii. p. 241.

1889. Freund: Samml. klin. Vorträge. Leipzig, 1889, Nos. 329 and 330.

1889. Saunsby: Illustrated Med. News. London, March 2, 1889

1889. Sollier: France médicale. 1889.

1889. Guinon: Gaz. des Hôpitaux. Nov. 9, 1889.

1889. Erb: Versamml. deutschen Naturforscher, med. Aerzte zu Heidelberg. September, 1889.

1889. Marie: Prog. médicale. No. 11, March 16, 1889. Translation in "Brain," 1889, vol. xii., p. 59.

1889. Farge: Prog. médicale. July 6, 1889.

1. 89. Adler: N. Y. med. Monatsschr. 1889, i., 225.

1889. Strümpell: Münch. med. Wochenschr., Aug. 15, 1889.

1889. Ewald: Berlin. klin. Wochenschr., March 18, 1889.

1889. Verstraeten: Rev. de Méd. May, 1889.

1889. Schultze: Deutsche med. Wochenschr. 1889, xv., 981.

1889. Gouraud: Paris, 1889.

1889. Hutchinson: Archives of Surgery. London, 1889-90, vol. i., p. 14.

1889. Schapovnikow: Med. Rundschau. 1889. (Russian.)

1889. Klebs: Die krankhaften Störungen, etc. 1889.

1889. Schaposchinkoff: Moskau, 1889.

1889. Sacchi: Venezia.

1890. Pechadre: Rev. de Méd. Paris, 1890.

1890. Holschewinkoff: Virchow's Archiv Bd. 119, 1890.

1890. Von Recklinghausen: Virchow's Archiv. Bd. 119, 1890.

1890. Waldo: Brit. Med. Journal. 1890.

1890. Thomson, J.: Anat. and Physiol. 1889-90, vol. xxiv., p. 475.

1890. Souza-Leite: De l'Acromegalie. Paris, 1890.

1890. Gauthier: Le Progrès médicale. 1890, No. 4.

1890. Renner: Vereine der pfälzischen Aerzte. Frankenthal, 1890.

1890. Graham: Trans. Assoc. American Physicians. 1890, vol. lvii.,p. 390.

1890. Graham: Medical News. Philadelphia, Oct. 18, 1890.

1890. Surmont: Nouvelle Iconograph de la Salpêtrière. Paris, 1890, iii., p. 147.

1890. Pick: Prag. med. Wochenschr. 1890, xv., p. 521.

1890. Campbell: Trans. Clinical Society London. 1890, xxiii., p. 257.

1890. Flemming: Trans. Clinical Society London. 1890, xxiii., p. 253.

1890. Silcock: Trans. Clinical Society London. 1890, xxiii., p. 256.

1890. Cénas: Loire Méd. 1890, ix., p. 313.

1890. Claus: Ann. Soc. de Méd. de Garad. 1890, lxix., p. 281.

1890. Gerhardt: Berlin. klin. Wochenschr. 1890, xxvii., p. 1183.

1890. Bettencourt: Jour. Soc. de Sc. méd, de Lsb. 1890, liv., 366.

1890. Holsti: Festski f. path.-anat. Inst. Helsingfor, 1890, 103.

1890. Souza-Leite: Rev. scient. Paris, 1890, xlvi., 801.

1890. Hutchinson: Archives Surgery. London, 1890, iv., 296.

1891. Paget: London Lancet. January 31, 1891.

1891. Cheron: Union méd. Paris, 1891, 3, s. 25.

1891. Leizet: Archive gén. de Méd. Paris. 1891, i., 194.

1891. Pel.: Berlin. klin. Wochenschr. 1891, xxviii., 53.

1891. Long: Lehigh Valley Medical Magazine. April, 1891, 144.

1891. Du Cazal: La Semaine médicale. October 21, 1891.

1891. Arnold: Beitr. f. path. Anatomie und zur allgemeiner Pathologie. Jena, 1891, x., p. 1.

1891. Pinel-Maisonneuve: Bul. et Mém. Soc. méd. de Hôp. de Paris. 1891, 3, s. viii., 137. Also, Archive d'Ophth., Paris, 1891, xi., 309.
1891. Groccu: Riv. gen. Ital. d. Clin med. Pisa, 1891, iii., p. 17.
1891. Mosler: Festschr. R. Virchow. Bd. ii., 103.
1891. Ruttle: Brit. Medical Journal. London, 1891, i., 697. Also, Medical Press and Circular, 1891, n. s., li., 397.
1891. Debierre: Rev. gén. d'Ophth. Paris, 1891, x., 12.
1891. Bury: Lancet. 1891, i., 1383.
1891. Kanthack: Brit. Medical Journal. 1891, ii., 188. Also, Trans. Path. Society London. 1890-91, xliii., 251.
1891. Marie et Marinesco: Archive de Méd. exper. et d'Anat. path. 1891, iii., 539.
1891. Berkley: Bul. Johns Hopkins Hospital. 1891, ii., 134.
1891. Somers: Occidental Medical Times. 1891, v., 537.
1891. Foy: Medical Press and Circular. London, 1891, n. s. liii., p. 491.
1891. Gorjatcheff: Chir. Laitof. Mosk., 1891, i., 155.
1891. Spellman et Haushalter: Rev. de Méd. 1891, xi., 775.
1891. Litthauer: Deutsche med. Wochenschr. Nov. 19, 1891.
1891. Bignani: Bul. d. Soc. Lancisiana d'Osp. d. Roma. 1891, x., 258.
1891. Gajkiewiczi: Gaz. Lekarska. Warszowa, 1891, 2, s. xi., p. 846.
1891. Stembo: St. Petersb. med. Wochenschr. 1891, Nos. 45 and 46.
1891. Bradford: Brit. Medical Journal. Dec. 26, 1891, 1354.
1891. Redmond: Trans. Royal Academy Ireland. 1890-91, ix., 64.
1892. Packard: Am. Journal Medical Sciences. June, 1892.
1892. Osborne: Am. Journal Medical Sciences. June, 1892.
1892. Duchesnau: Contribution à l'Étude anatomique et chir. de l'Acromegalie, etc. 4°, Lyon, 1892.
1892. Möbius: Münch. med Wochenschr. June 9, 1892.
1892. Tanzi: Archivio Ital. d. Clin. med., v., p. 533; Gaz. degli Ospit., No. 9, 1891.
1892. Appleyard: Lancet. 1892, i., 316.
1892. ——: Lancet. 1892, i., 746.
1892. Balzer: Bul. et Mém. Soc. méd. d'Hôp. de Paris. 1892, 3, s. ix., 237.
1892. Bard.: Lyon méd. 1892, lxix., 547.
1892. Phillips: Brit. Medical Journal. Feb. 27, 1892.
1892. Barrs: Lancet. 1892, i., 683.
1892. Gonzalez-Cepeda: Rev. Balear de Cien. med. Palma de Mallorca, 1892, viii., 7.
1892. Hare: Medical News. Philadelphia, 1892, lx., 257.
1892. Hutchinson: Archives Surgery. 1891-92, iii., 343.
1892. Solis-Cohen: Medical News. Philadelphia, Nov. 5, 1892.
1892. Harris: Medical News. Philadelphia, Nov. 5, 1892.
1892. Dulles: Medical News. Philadelphia, Nov. 5, 1892.
1892. Brown: Brit. Medical Journal. April 23, 1892.
1892. Barclay and Symmers: Brit. Medical Journal. Dec. 3, 1892.
1892. Denti: Atti d'Asso. Lombardi. Milano, 1891-92, 41.
1892. Sarbo: Orbosi hetit. Budapest, 1892, xxxvi., 136.
1892. Orsi: Gaz. med. Lombard. 1892, li., 201.
1892. Boltz: Deutsche med. Wochenschr. 1892, xviii., 635.
1892. Fratrich: Allgemeine Wiener Zeitung. 1892, xxxvii., 405.
1892. Holsti: Zeitschrift f. klin. Med. 1892, xx., 298.
1892. Massalongo: Rif. med. Napoli. 1892, viii., part 3, 74.
1892. Buzer: Aerztl. Rundschau. München, 1892, ii., 509.
1892. Mosler: Wiener Med.-Blatt. 1892, xv., 56, 70, 87, 105, 121, 136.
1892. Bruzzi: Gaz. d'Osp. Milano, 1892, xiii., 866.
1892. Gause: Deutsche med. Wochenschr. 1892, xviii., 891.